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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/052,121	01/17/2002	Cato T. Laurencin	DRE-0067	1682

7590 11/30/2006

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EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1657	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,121	LAURENCIN ET AL.	
	Examiner	Art Unit	
	David M. Naff	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment of 8/29/06 in response to an office action of 5/31/06 amended claim 1.

Claims examined on the merits are 1-3, 5 and 6, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Starling et al (6,210,715 B1) in view of Crotts et al (Journal of Controlled Release) for reasons set forth in the previous office action of 5/31/06 and for reasons herein.

The claim is drawn to scaffold for tissue engineering comprising biodegradable polymer-based hollow microcarriers with a density equal to or less than water bonded together by heating at several degrees above the glass transition temperature of the polymer into a three dimensional scaffold with a density equal to or less than water and a fully interconnected pore network. The scaffold exhibits cell attachment and retains cell phenotype upon in vitro culturing with cells in a rotating bioreactor.

Starling et al disclose microcarriers (also referred to as microspheres or microbeads) that can be used for cell culture (col 4, lines 32-35, col 5, lines 1-7 and col 6, lines 32-35), or as an implant as a carrier of a pharmaceutical agent (col 9, lines 15 and 22, and col 9, line 57). The microspheres can be hollow, and be

bonded together to form an aggregate of bonded together hollow microspheres (Figure 1-1 (1.4)). The hollow microspheres have a density of less than 1 gm/cc (col 6, line 54), and are bonded together by coating with calcium phosphate (CaP) and sintering to provide an aggregate having a density of about 1.00-1.12 gm/cc (col 6, line 60), preferably about 1.00-1.06 gms/cc (col 4, line 58). The hollow microspheres are made of a substrate, which can be calcium phosphate, glass, other oxide ceramics or polymers, proteinaceous materials or composite materials (col 5, line 66 to col 6, line 2). When the substrate material is polymeric or proteinaceous, bonding together of the hollow microspheres can involve heating the substrate material to soften the surface (col 6, lines 44-46). Polymeric/organic substrate materials for preparing the hollow microsphere include dextran, polyethylene, polypropylene, polystyrene, polyurethane and collagen (col 17, lines 36-39).

Crotts et al disclose preparing hollow microspheres composed of poly(D,L-lactic-co-glycolic acid) (PLGA) (page 91, abstract) that can be used as a carrier for drug delivery by encapsulating a drug (page 104, right col, lines 1-11). Poly(D,L-lactic acid) and its copolymers with glycolic acid are used as microsphere material due to their versatile biodegradability and biocompatibility (page 91, left col, under "Introduction"). The microspheres are prepared (page 93, left col, under "Microsphere preparation") by adding a water phase (with or without BSA (blood serum albumin)) to methylene chloride containing PLGA, generating an emulsion by ultrasonication, adding the emulsion

to a PVA/PBS solution while being magnetically stirred, and continuing stirring for 2-3 h to permit evaporation of solvent. The microspheres are collected by centrifugation, washed and lyophilized, and size distribution is measured by using a series of stainless steel meshes.

It would have been obvious to use as the polymeric hollow microspheres of Starling et al, hollow microspheres made from PLGA as suggested by Crotts et al to obtain the property of PLGA having versatile biodegradability and biocompatibility as disclosed by Crotts et al. It would have been expected the PLGA hollow microspheres can be bonded together to form an aggregate of hollow microspheres by procedures disclosed by Starling et al. The aggregate when shaped as disclosed by Starling et al (col 9, lines 50-58) will be a scaffold as presently claimed. Heating to soften the surface of microspheres to bond the microspheres together as suggest by Starling et al will result in using a temperature several degrees above the polymer glass transition temperature of the polymer. A scaffold resulting from modifying Starling et al as suggested by Crotts et al will inherently retain phenotype when culturing in vitro in a rotating bioreactor as claimed.

Response to Arguments

The amendment argues that Starling et al must coat the microspheres with CaP. While coating with CaP may be preferred by Starling et al, coating can be omitted when bonding polymeric microspheres together by softening as disclosed by Starling et al since a function of the CaP is to bond the microspheres together.

While Starling et al disclose that a function of the CaP coating on non-CaP substrates is to enhance beneficial bioactivity of the substrate surface in cell culturing applications, this enhancement is not critical to Starling et al. This is further apparent from Starling et al disclosing (col 3, lines 35-40) that the microbeads can contain 0-100% tricalcium phosphate and/or 0-100% calcium phosphate compounds. These ranges encompass 0%, and a CaP coating does not result in 0% calcium phosphate compounds. Further see col 4, lines 1-3 where it is disclosed that the invention provides polymer microbeads formed with or coated with HA, TCP and other CaPs. This further indicates that the coating of Starling et al can be omitted. In any event, the present claims do not exclude the microcarriers from being coated with CaP since the claims recite "polymer-based hollow microcarriers". This recitation permits the microcarriers to contain materials other than a polymer even though claim 1 recites "consisting" in line 2.

It is granted that that Crotts et al teach microspheres for controlled drug release instead of microspheres in aggregates for cell culture. However, the microspheres of Starling et al like those of Crotts et al can be made of a polymer, and due to the similarity of the polymer microspheres, it would have been expected the microspheres of Crotts et al will provide an aggregate by heating to soften the surface as disclosed by Starling et al. Furthermore, it would have been obvious to use the PLGA polymer of Crotts et al because of its versatile biodegradability and biocompatibility as the polymer used by

Starling et al to prepare microspheres without forming a microsphere containing a drug as disclosed by Crotts et al.

While the omission of an element and retaining its function may be unobvious as urged in the amendment, there is inadequate evidence to establish that the microcarriers of the claims when made of only a polymer have all the functions disclosed by Starling et al when a CaP coating is present.

Claim Rejections - 35 USC § 103

Claims 2, 3, 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over the references as applied to claim 1 above, and further in view of Spaulding (6,001,643) or Granet et al (AJ on 1449).

Claims 2 and 3 require the scaffold of claim 1 to be seeded with cells via culturing *in vitro* in a rotating bioreactor.

Claims 5 and 6 require a method of generating tissue by seeding the scaffold of claim 1 with cells that produce the tissue, and culturing the seeded cells in a rotating bioreactor.

Starling et al and Crotts et al are described above.

Spaulding discloses culturing cells in a roller bottle for implanting to produce tissue. Microcarrier beads having densities less than the cell culture medium can be used for cell attachment to constrain tissue constructs to the area surrounding the annular axis and away from the cylinder wall of the bottle (col 16, lines 25-30).

Granet et al disclose culturing osteoblastic cells on microcarriers in a rotating-wall vessel (page 514, section 2.1.2).

When preparing the aggregate of bonded together hollow microspheres of Starling et al using hollow microspheres made from PLGA as suggested by Crotts et al as set forth above, it would have been obvious to use the aggregate for cell culture as suggested by Starling et al, and carry out cell culture in a roller bottle as disclosed by Spaulding or in a rotating-wall vessel as disclosed by Granet et al since these culturing techniques are intended for culturing cells on a carrier. It would have been further obvious to provide the aggregate with a density less than that of water as suggested by Spaulding so the aggregate will surround the axis away from the wall. Culturing cells such as osteoblast cells would have been obvious when the function of these cells is desired.

Response to Arguments

This rejection has not been separately traversed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

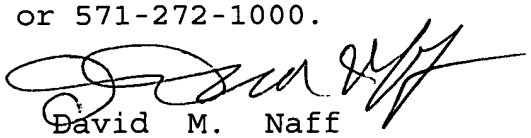
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



David M. Naff
Primary Examiner
Art Unit 1657

DMN
11/27/06